

CARTA CIENTÍFICO-CLÍNICA

[Translated article] Extensive White Sponge Nevus

Nevus blanco esponjoso extenso

To the Editor,

A healthy 5-month-old boy, with no relevant family history and an unremarkable pregnancy and delivery was evaluated due to the presence of whitish plaques located on the external and internal oral mucosa (fig. 1), which the parents reported as congenital. He exhibited a white-yellowish plaque affecting the external labial mucosa, and whitish, velvety plaques that did not detach with friction were observed on the lateral lingual mucosa and buccal mucosa. No other abnormalities were observed in the nails, hair, skin, or mucous membranes. He also did not present with stridor either. Neither parent had similar lesions. A laryngoscopy under sedation ruled out respiratory tract involvement. A biopsy of the buccal lesions revealed the presence of an acanthotic mucosa with clear cytoplasm keratinocytes, intracellular edema, and isolated dyskeratotic cells (fig. 2).



No alterations were detected in the molecular study either. For the genetic study, the human exome was sequenced using Illumina DNA Prep with Exome v2.0 PLUS Enrichment with a total coverage of 37.5 Mb from a peripheral blood DNA sample. The Geneyx analysis software was used for tertiary test based on the following HPO phenotypes: nevus, white sponge nevus, and pachyonychia congenita. Additionally, the KRT13, KRT4, KRT6A, and KRT6B genes were specifically reviewed. Based on the clinical-histopathological findings and the absence of other associated signs, a diagnosis of white sponge nevus (WSN) was established.

WSN is a rare disease of autosomal dominant inheritance and variable penetrance and expressivity^{1,2}. Germline mutations in the keratin 4 and 13 genes have been isolated in patients with this condition. Despite this, Liu et al. conducted a molecular study on peripheral blood in 5 patients with sporadic WSN, and only 1 was found to have a mutation in 1 of these cytokeratins, as opposed to the 3 patients with familial WSN analyzed, all of whom had mutations in keratin 4 or cytokeratin 13^{3,4}.

The most common location is the buccal mucosa, followed by other parts of the oral or labial mucosa. However, it can also damage the esophagus, respiratory tract, rectum,

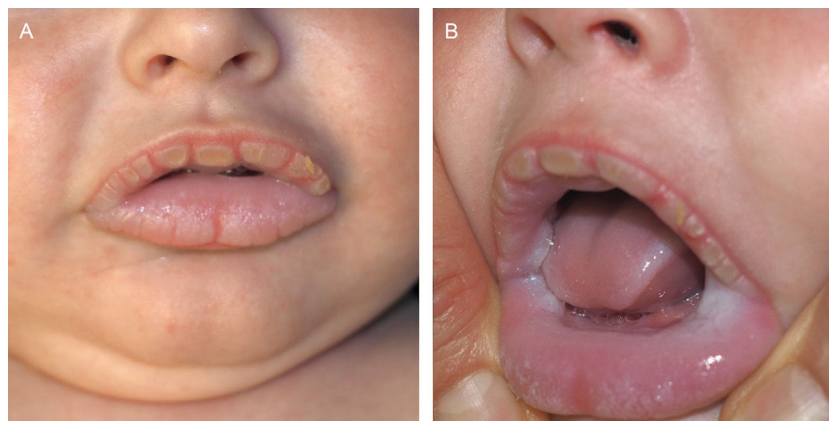


Figure 1 Hyperkeratotic white-yellowish plaques affecting the entire external labial mucosa (A). Bilateral and symmetrical whitish velvety plaques on the buccal, internal labial, and lateral lingual mucosae (B).

DOI of original article:
<https://doi.org/10.1016/j.ad.2023.01.027>

<https://doi.org/10.1016/j.ad.2024.08.002>

0001-7310/© 2023 AEDV. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

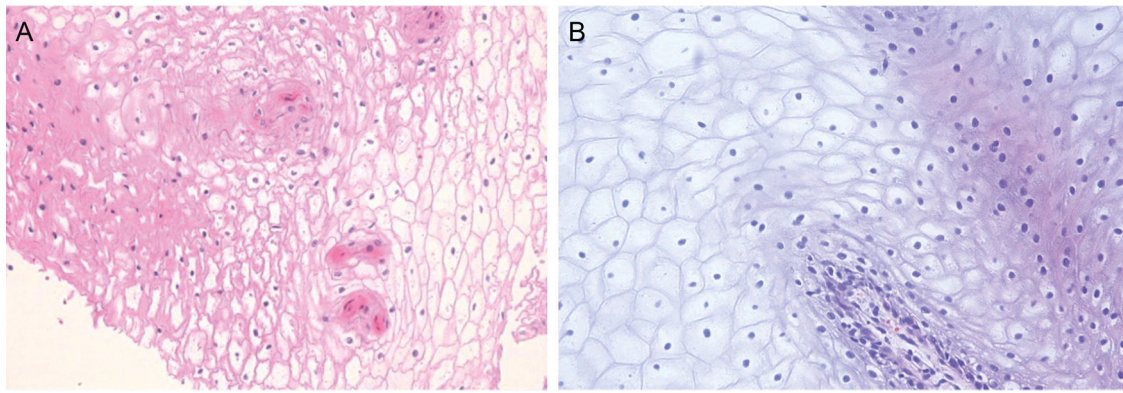


Figure 2 Biopsy of the buccal mucosa showing mainly acanthosis, intracellular edema in keratinocytes, and dyskeratosis (HE).

Table 1 Differential diagnosis of leukoplakia in childhood.

Pachyonychia congenita ⁶	Benign hereditary intraepithelial dyskeratosis ⁷	Congenital dyskeratosis ⁸
Mutations in cytokeratins: 6A, 6B, 6C, 16, and 17	Corneal dystrophy	Associated with telomeric alterations. Higher number of pathogenic mutations in the DKC1 gene, followed by RTEL1 and TERT Predominantly in males
Palmoplantar keratoderma	Whitish lesions on the bulbar conjunctiva and oral mucosa	Reticulated hyperpigmentation (possible hypopigmentation, atrophy, poikiloderma) Nail dystrophy Leukoplakia Involvement of other organs: bone marrow, lungs, liver
Laryngeal involvement	Conjunctival hyperemia	
Subungual hyperkeratosis Hyperhidrosis Oral leukoplakia		
Epidermal cysts or multiple steatocystomas		

or genitals. Clinically, it shows as thickened, whitish, bilateral, and symmetrical plaques with a velvety surface that do not disappear with friction^{2,5}. Histopathologically, it is characterized by the presence of acanthosis, hyperparakeratosis, vacuolization of keratinocytes in the suprabasal layers, and occasionally perinuclear eosinophilic deposits of cytokeratin tonofilaments.

Although WSN often develops in early childhood, with a clinical diagnosis, it can also be detected in adults, for whom histopathological tests are advised to rule out the presence of any other possible etiologies¹. In children, candidiasis should be ruled out and differentiated from other entities such as pachyonychia congenita, benign hereditary intraepithelial dyskeratosis, and congenital dyskeratosis (Table 1). If WSN is suspected in adulthood, the differential diagnosis should include lichen planus, squamous cell carcinoma, linea alba, frictional leukoplakia, Darier disease, lupus erythematosus, or secondary syphilis^{1,2}.

Multiple treatments with variable effectiveness for WSN have been described, such as topical or oral tetracyclines, surgery, CO₂ laser, beta-carotenes, chlorhexidine rinses, and others. The therapeutic goal is primarily aesthetic since it is a benign and asymptomatic condition^{2,3}.

In conclusion, a sporadic WSN with extensive involvement of the oral mucosa has been described. Notably, there was significant involvement of the external labial mucosa, which is uncommon for this entity.

Conflicts of interest

None declared.

References

- Bezerra KT, Leite TC, Roza ALOC, Araújo R, Israel MS, Canedo NHS, et al. White sponge nevus: A condition not always clinically suspected. *J Cutan Pathol.* 2020;47:22–6.
- Elfatoiki FZ, Capatas S, Skali HD, Hali F, Attar H, Chiheb S. Oral white sponge nevus: An exceptional differential diagnosis in childhood. *Case Rep Dermatol Med.* 2020;2020, 9296768.
- Amores-Martín E, Melé-Ninot G, del Alcázar Viladomiu E, Fernández-Figueras MT. Successful treatment of white sponge nevus with oral doxycycline: A case report and review of the literature. *Actas Dermosifiliogr.* 2021;112:463–6.
- Liu X, Li Q, Gao Y, Song S, Hua H. Mutational analysis in familial and sporadic patients with white sponge naevus. *Br J Dermatol.* 2011;165:448–51.

5. Sobhan M, Alirezaei P, Farshchian M, Eshghi G, Ghasemi Basir HR, Khezrian L. White sponge nevus: Report of a case and review of the literature. *Acta Med Iran.* 2017;55:533–5.
6. Koprulu M, Naeem M, Nalbant G, Shabbir RMK, Mahmood T, Huma Z, et al. KERATIN 17-related recessive atypical pachyonychia congenita with variable hair and tooth anomalies. *Eur J Hum Genet.* 2022;30:1292–6.
7. Bui T, Young JW, Frausto RF, Markello TC, Glasgow BJ, Aldave AJ. Hereditary benign intraepithelial dyskeratosis: Report of a case and re-examination of the evidence for locus heterogeneity. *Ophthalmic Genet.* 2016;37:76–80.
8. AlSabbagh MM. Dyskeratosis congenita: A literature review. *J Dtsch Dermatol Ges.* 2020;18:943–67.

A. Llull-Ramos*, I. Gracia-Darder, A. Martín-Santiago

Servicio de Dermatología, Hospital Universitario Son Espases, Palma, Islas Baleares, Spain

*Corresponding author.

E-mail address: anallullramos@gmail.com (A. Llull-Ramos).